

### **REMARKS**

Claims 1-13 are pending in this application. Claims 9-13 have been withdrawn from consideration as being drawn to non-elected subject matter. Claims 1, 6, and 8 have been amended.

#### **Amended Claims 1, 6, and 8.**

Claims 1, 6 and 8 have been amended to clarify that the claims are directed to an enzymatically active heterodimer comprising hsGC $\alpha$ 1 (SEQ ID NO: 2) and hsGC $\beta$ 1 (SEQ ID NO: 4). Claim 1 was also amended to remove the phrase "purified to apparent homogeneity." Support for these amendment is found, for example, on page five lines 9-13, page 9, line 18 through page 10, line 19, and Figures 10-12. No new matter is added by these amendments.

#### **Amendments to the Specification.**

The specification was amended to add a cross-reference to identify this application as a National Stage of the PCT and to add sequence identifier numbers (SEQ ID NO) where necessary to comply with Rule 1.821(d). A substitute Sequence Listing including the sequence identifiers added in the present amendment is enclosed herewith. Applicants request that the specification be amended to enter the attached paper copy of this substitute Sequence Listing. No new matter is added by these amendments or the substitute Sequence Listing.

#### **The Claims Are in Compliance with the Second Paragraph of 35 USC §112.**

Claim 1 was rejected as purportedly being indefinite due to the phrase "purified to apparent homogeneity". This term is widely used in the art and would be readily understandable to one of ordinary skill to mean that the protein appears as a single band in a gel electrophoretogram. Nonetheless, the current amendment to claim 1 deletes this phrase, so this ground for rejection is moot.

Claims 1, 6 and 7 were rejected as purportedly failing to particularly point out and distinctly claim the subject matter that the applicant regards as his invention. In particular the phrase "guanylyl cyclase  $\alpha$ 1 (hsGC $\alpha$ 1; SEQ ID NO: 2)/ $\beta$ 1 (hsGC $\beta$ 1; SEQ ID NO: 4)" was objected to as being unclear. This phrase has been eliminated from claims 1 and 6 and is

replaced by the phrase "guanylyl cyclase  $\alpha 1/\beta 1$ , which is an enzymatically active heterodimer comprising hsGC $\alpha 1$  (SEQ ID NO: 2) and hsGC $\beta 1$  (SEQ ID NO: 4)." This amendment is meant to clarify that the claimed product is a heterodimeric enzyme that is composed of two specifically identified protein subunits. Applicants believe that the scope of claims 1 and 6, as well as claim 7, which depends on claim 6, is clear. Although not included in the rejection, claim 8 has been amended in the same manner as claims 1 and 6 for consistency.

**Claims 1 and 2 Are Not Anticipated by the Applied References.**

Claim 1 has been rejected as allegedly being anticipated by Giuli *et al.* This rejection is unwarranted. Claim 1 is directed to a human guanylyl cyclase  $\alpha 1/\beta 1$ , which is an enzymatically active heterodimer comprising hsGC $\alpha 1$  (SEQ ID NO: 2) and hsGC $\beta 1$  (SEQ ID NO: 4). Although Giuli *et al.* purport to describe certain  $\alpha$  and  $\beta$  subunits of human guanylyl cyclase, the reference does not describe an enzymatically active heterodimer of hsGC $\alpha 1$  (SEQ ID NO: 2) and hsGC $\beta 1$  (SEQ ID NO: 4). In fact, the sequence for the  $\alpha$  chain reported by the reference (see Fig. 2 of Giuli *et al.*) is not the same sequence as that of hsGC $\alpha 1$  (SEQ ID NO: 2) of the present application. As pointed out in the specification of the present application, on page 19, lines 18-31 and in FIG. 3, the DNA sequence for the hsGC $\alpha 1$  chain reported by Giuli *et al.* differs considerably from SEQ ID NO: 2. The amino acid sequence for the  $\alpha$  chain in Fig. 2 of Giuli *et al.* includes 717 amino acid residues, whereas SEQ ID NO: 2 includes only 690 residues. In addition, the sequence in Fig. 2 of Giuli *et al.* differs from that of SEQ ID NO: 2 beginning with amino acid residue 124 and continuing through the end of the sequence. Accordingly, Giuli *et al.* does not teach or suggest the human guanylyl cyclase  $\alpha 1/\beta 1$  that is presently claimed. This rejection should be withdrawn.

Claim 1 and 2 were rejected as being anticipated by Zabel *et al.* This rejection is also unwarranted. Zabel *et al.* has a publication date of October 1, 1998, which is after the filing date of the priority application, DE 195 37 015.6, which was filed on August 14, 1998 (see the PubMed printout listing the publication date of this reference, enclosed herewith).

Accordingly, Zabel *et al.* is not available as a reference against the present application. Furthermore, Zabel *et al.* is the work of the present inventors Zabel and Schmidt, published *less than one year* before filing of the PCT application from which the present application claims priority. Hence, Zabel *et al.* is not be available as a reference against this application under 35 U.S.C. 102(a) either.

**Claims 3-8 Are Not Obvious Over the Applied References.**

Claims 3-8 have been rejected as purportedly being obvious over either Zabel *et al.* or Giuli *et al.* and further in view of common knowledge in the art regarding methods of affinity chromatography using affinity tags for protein purification. This rejection is also unwarranted. As noted above, Zabel *et al.* is not available as a reference against the present application and Giuli *et al.* does not teach or suggest the same  $\alpha$  subunit as hsGC $\alpha$ 1 (SEQ ID NO: 2) of the present application. Even assuming common knowledge regarding purification using affinity tags, the combination of Giuli *et al.* with this common knowledge cannot render claims 3-8 obvious, since Giuli *et al.* does not teach or suggest the human guanylyl cyclase  $\alpha$ 1 subunit of SEQ ID NO: 2, which is a material limitation of all of the claims.

Accordingly, all of the present claims are deemed to be patentable over the applied references. The objections to the specification have been addressed by appropriate amendments and submission of a substitute Sequence Listing. An early allowance of all claims is solicited.

Respectfully submitted,

Dated

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